

APPLICANT(S): CAPPOLA, Thomas. *et al.*

SERIAL NO.: 10/587,569

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AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning at line 24 of page 27 as follows:

The analysis was carried out using robust multi-array analysis (RMA), since small data sets were analyzed. Software for RMA is available online at the website www.bioconductor.org, for use in the R 1.70 package for statistical computing (www.r-project.org).

Please amend the paragraph beginning at line 1 of page 28 as follows:

To determine candidate markers of rejection, three criteria were applied to the normalized data. First, data were filtered to include genes present above background on at least one array. Second, Significance Analysis of Microarrays (SAM; http://www-stat.stanford.edu/~tibs/SAM/) was used to correct for multiple comparisons and to select candidate markers of rejection using genes that were differentially expressed with an estimated overall false-discovery rate <0.10. Third, we required at least a 25% change in expression between Rejection and Control samples for a transcript to be of interest. The identities of differentially expressed genes were determined using annotation databases (www.netaffx.com) or via BLAST searches of the corresponding expressed sequence tags.

Please amend the paragraph beginning at line 13 of page 28 as follows:

To determine whether candidate markers of rejection responded to immunosuppressive therapy, expression data was analyzed for these transcripts in patient samples, which were isolated from patients who had rejected the cardiac allografts. These samples were assessed in order to determine whether the expression pattern of the candidate genes paralleled what was seen in the subjects at baseline. [is this correct?]

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Please amend the paragraph beginning at line 3 of page 29 as follows:

The capacity of candidate markers to distinguish Control, Rejection, and Post-Rejection samples was assessed using hierarchical clustering. Clusters were constructed using average linkage clustering and Pearson correlation coefficients as a measure of similarity using Cluster software and displayed using Treeview software (<http://rana.lbl.gov>).

Please amend Table 2 beginning at line 7 of page 33 as follows:

Table 2. Candidate Expression Markers of Cardiac Allograft Rejection

Gene (Gene Symbol)	Protein Type/ Cellular Pathway	Fold-Change (Rejection versus Control)	Fold-Change (Post- Rejection versus Control)	Probe-Set ID*	UniGene ID†
ubiquinol-cytochrome c reductase binding protein (UQCRB)	Oxidative respiration	2.25	1.3	205849_s_at	Hs.131255
basic transcription factor 3 (BTF3)	RNA translation	1.57	1.24	208517_x_at 211939_x_at	Hs.446567
suppression of tumorigenicity 13 (ST13)	Tumor suppressor	1.43	1.19	207040_s_at	Hs.377199
cullin 4A (CUL4A)	Cell cycle/DNA replication	1.34	1.1	201423_s_at	Hs.270788
telomeric repeat binding factor 2, interacting protein (TERF2IP)	Transcription factor	1.31	1.15	201174_s_at	Hs.274428
arrestin, beta 2 (ARRB2)	Intracellular signaling	0.75	0.79	203388_at	Hs.435811
EST		0.75	0.99	207365_x_at	Hs.435123
EST		0.74	0.96	207730_x_at	Hs.406701
EST		0.74	0.86	205781_at	Hs.164410

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aminopeptidase puromycin sensitive (NPEPPS)	Proteinase	0.73	0.91	201454_s_at	Hs.293007
phosphatidylinositol glycan, class B (PIGB)	Cell surface protein	0.73	0.8	205452_at	Hs.259326
adenomatosis polyposis coli (APC)	Tumor suppressor	0.72	0.9	216933_x_at	Hs.75081
B-cell CLL/lymphoma 7A (BCL7A)	Cell cycle/DNA replication	0.72	0.98	210679_x_at	Hs.371758
endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4 (EDG4)	Cell cycle/DNA replication	0.72	0.81	206722_s_at 206723_s_at	Hs.122575
interleukin 17 receptor (IL17R)	Interleukin receptor	0.72	0.79	205707_at	Hs.129751
placental growth factor (PGF)	Hormone/ Angiogenesis Factor	0.72	0.96	215179_x_at	Hs.252820
EST		0.7	0.85	220712_at	Hs.493129
EST		0.7	0.9	215558_at	Hs.485406
EST		0.7	0.9	220071_x_at	Hs.14347
nuclear factor of activated T-cells 5, tonicity-responsive (NFAT5)	Transcription factor	0.7	0.83	208003_s_at	Hs.86998
EST		0.69	0.89	221205_at	
EST		0.69	0.89	215978_x_at	Hs.447720
baculoviral IAP repeat-containing 1 (BIRC1)	Apoptosis	0.68	0.76	204861_s_at	Hs.79019
leukocyte immunoglobulin-like receptor, subfamily B, member 3 (LILRB3)	Leukocyte receptor	0.68	0.81	210784_x_at 211135_x_at	Hs.306230
EST		0.66	0.94	209703_x_at	Hs.288771
transmembrane 6 superfamily member 2 (TM6SF2)	Cell surface protein	0.66	0.88	210598_at	Hs.367829
EST		0.65	0.9	215375_x_at	Hs.438377
EST		0.65	0.94	215029_at	Hs.293563

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CASP8 and FADD-like apoptosis regulator (CFLAR)	Apoptosis	0.59	0.73	211862_x_at 210564_x_at 208485_x_at 211317_s_at 214486_x_at	Hs.355724
superoxide dismutase 2, mitochondrial (SOD2)	Oxidative stress	0.56	0.83	221477_s_at	Hs.384944
EST		0.55	0.84	216109_at	Hs.435249
solute carrier family 16, member 3 (SLC16A3)	Membrane transport	0.54	0.66	202856_s_at	Hs.386678
stearoyl-CoA desaturase 4 (SCD4)	Fatty acid metabolism	0.5	0.87	220232_at	Hs.379191
*Probe-Set ID: indicates the corresponding probe-set on the Affymetrix HU 133A microarray— http://www.affymetrix.com					
†Unigene ID information are available online at NCBI website. : http://www.ncbi.nlm.nih.gov/UniGene					
EST indicates Expressed Sequence Tag					